

FIGURE 1

| PHASE I HCV TRIAL: STUDY PROTOCOL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-----------------------------------|---|--------------------|---|---|---|---|---|---|---|---|----|-----------------|----|----|----|----|----|----|----|----|----|------------|----|----|----|----|---|--|--|--|
| WEEK: | 0 | IV+ORAL TREATMENT: | | | | | | | | | | ORAL TREATMENT: | | | | | | | | | | FOLLOW UP: | | | | | | | | |
| ORAL TREATMENT | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 24 | 28 | 32 | 36 | 40 | | | | |
| | | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | x | | | | | | | | | |
| | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | | | | | | | | | | | | | | | |
| PHYSICIAN VISIT | x | x | x | x | x | x | x | x | x | x | x | | x | | x | | x | | x | | x | | x | x | x | x | x | | | |
| SMA (6) | x | | | | | | | | | x | | | x | | | | x | | | | x | | x | | x | | | | | |
| CBC | x | | | | | | | | | x | | | x | | | | x | | | | x | | x | | x | | | | | |
| HCV-PCR RNA | x | | | | | | | | | x | | | x | | | | x | | | | x | | x | | x | | | | | |
| QUANTITATIVE | | | | | | | | | | x | | | x | | | | x | | | | x | | x | | x | | | | | |
| ANTI HCV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI HCV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CONFIRMATION | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HCV-PCR | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GENOTYPE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CRYOGLOBULINS | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| LIVER BIOPSY | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ABDOMINAL US | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PT, PTT | x | | | | | | | | | x | | | x | | | | x | | | | x | | x | | x | | | | | |
| AFP | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| NH3 | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ESR | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANF | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| C3 | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| MITOCHONDRIA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI SMOOTH | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| MUSCLE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI PARIETAL | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CELL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| IEP | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HIV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| HBSAG | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANIT HBC | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI HAV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI CMV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ANTI EBV | x | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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FIGURE 2

SCORING & GRADING SYSTEMS

Table 1. HAI for numerical scoring of liver biopsy specimens

| I. Periportal +/- Bridging Necrosis | Score | II. Intralobular Degeneration* and Focal Necrosis | Score | III. Portal Inflammation | Score | IV. Fibrosis | Score |
|--|-------|--|-------|--|-------|--|-------|
| A. None | 0 | A. None | 0 | A. No portal inflammation | 0 | A. No fibrosis | 0 |
| B. Mild piecemeal necrosis | 1 | B. Mild (acidophilic bodies, ballooning degeneration and/or scattered foci of hepatocellular necrosis in <1/3 of lobules or nodules) | 1 | B. Mild (sprinkling of inflammatory cells in <1/3 of portal tracts) | 1 | B. Fibrous portal expansion | 1 |
| C. Moderate piecemeal necrosis (involves less than 50% of the circumference of most portal tracts) | 3 | C. Moderate (involvement of 1/3-2/3 of lobules or nodules) | 3 | C. Moderate (increased inflammatory cells in 1/3- 2/3 of portal tracts) | 3 | C. Bridging fibrosis (portal-portal or portal- central linkage) | 3 |
| D. Marked piecemeal necrosis (involves more than 50% of the circumference of most portal tracts) | 4 | D. Marked (involvement of >2/3 of lobules or nodules) | 4 | D. Marked (dense packing of inflammatory cells in >2/3 of portal tracts) | 4 | D. Cirrhosis† | 4 |
| E. Moderate piecemeal necrosis <i>plus</i> bridging necrosis‡ | 5 | | | | | | |
| F. Marked piecemeal necrosis <i>plus</i> bridging necrosis‡ | 6 | | | | | | |
| G. Multilobular necrosis§ | 10 | | | | | | |

NOTE. HAI score is the combined scores for necrosis, inflammation, and fibrosis.

*Degeneration—acidophil bodies, ballooning; focal necrosis—scattered foci of hepatocellular necrosis.

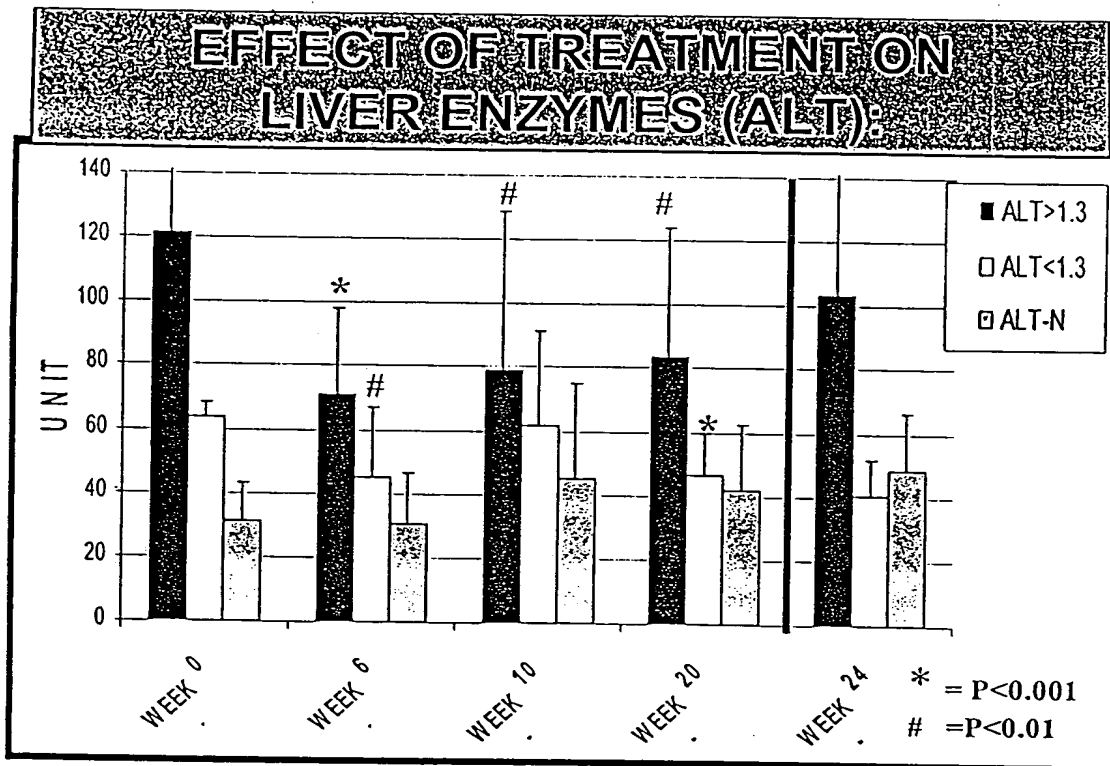
†Loss of normal hepatic lobular architecture with fibrous septae separating and surrounding nodules.

‡Bridging is defined as ≥ 2 bridges in the liver biopsy specimen; no distinction is made between portal-portal and portal-central linkage.

§Two or more contiguous lobules with panlobular necrosis.

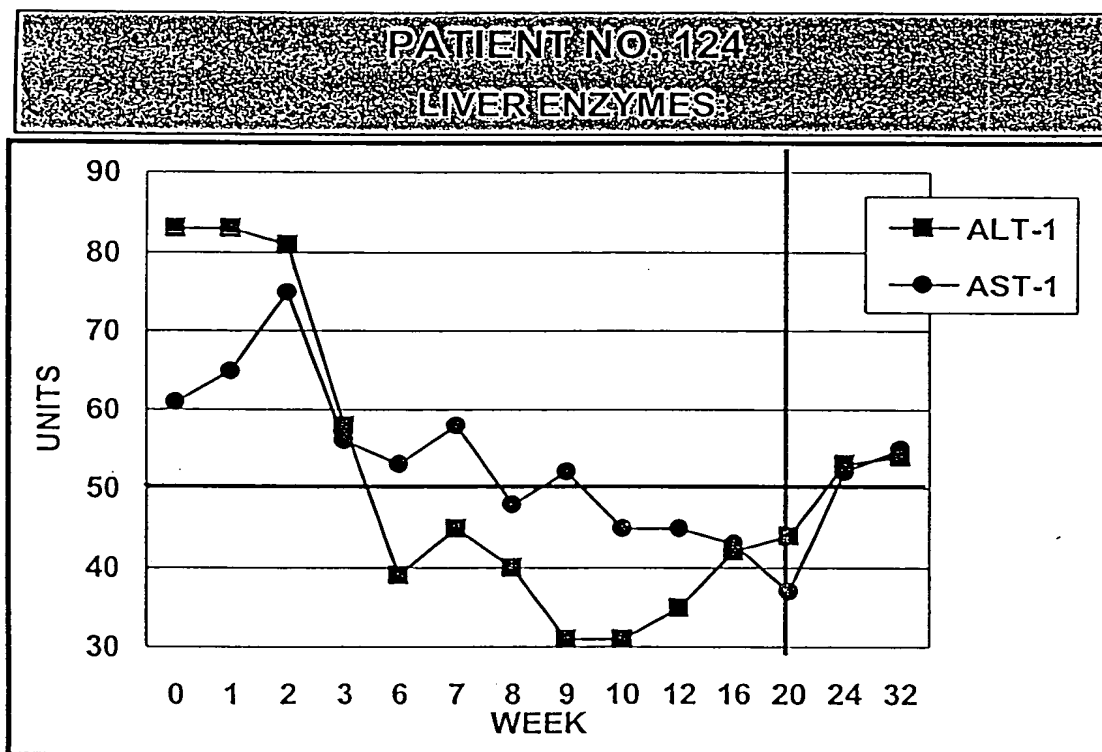
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FIGURE 3



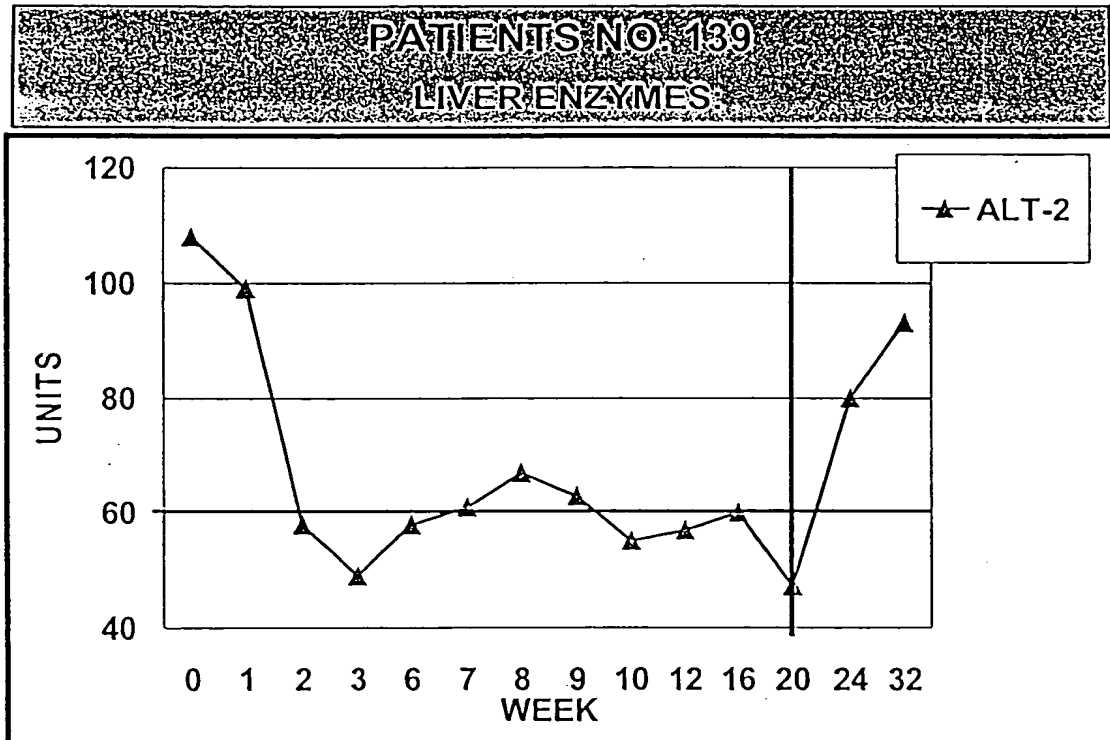
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FIGURE 4



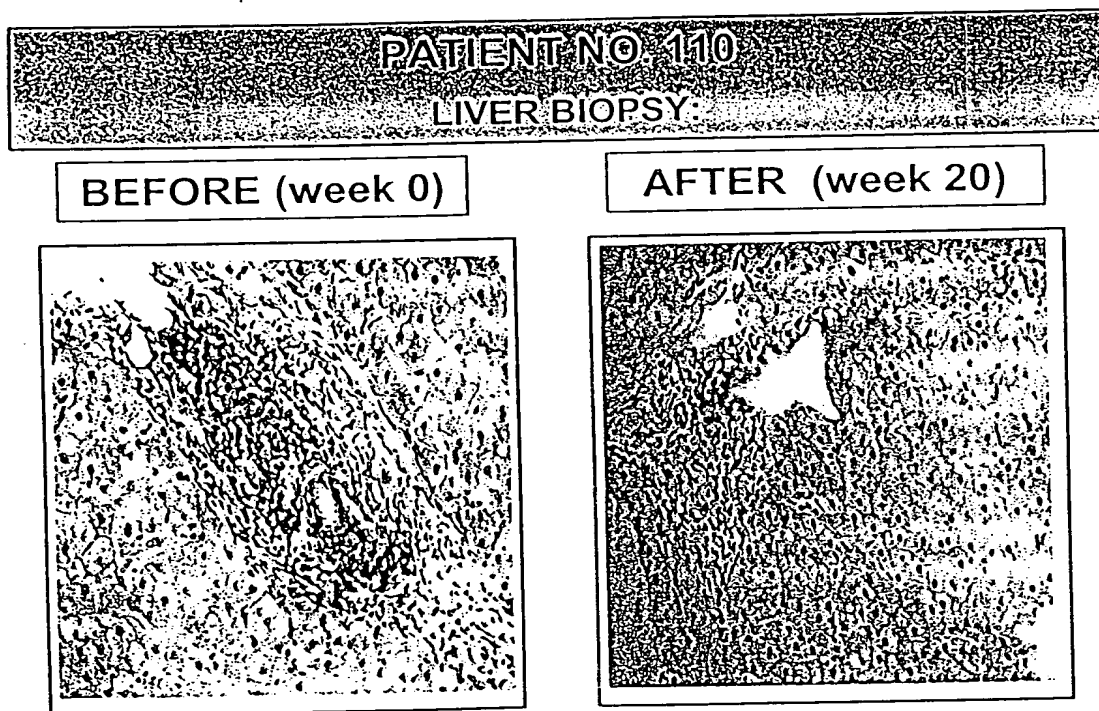
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FIGURE 5



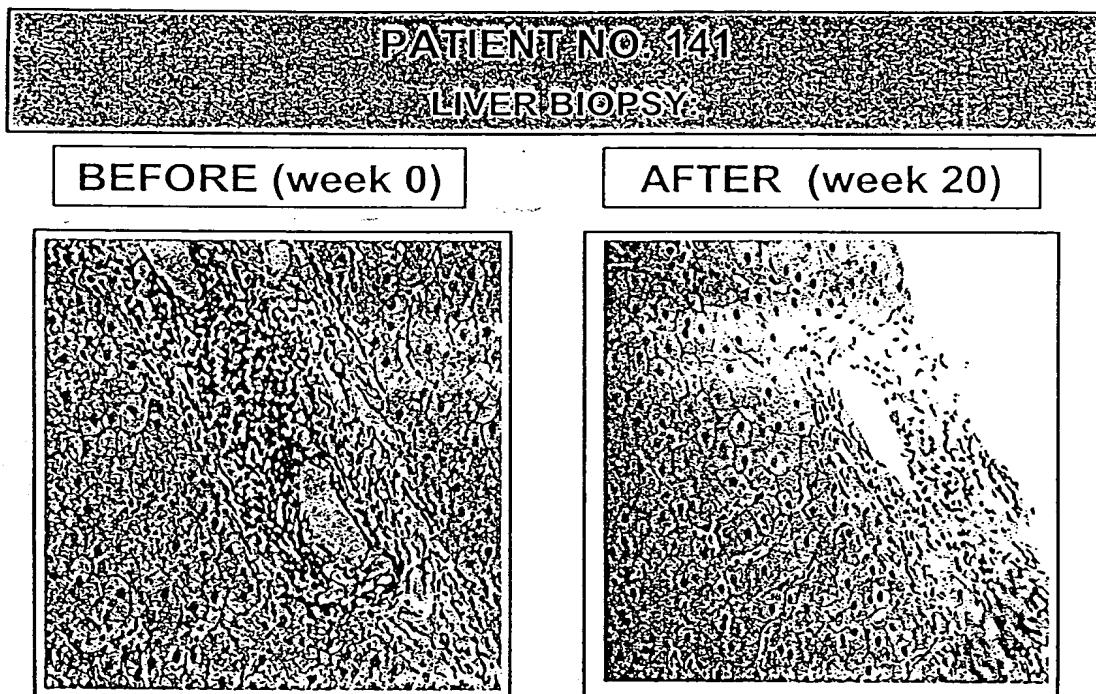
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FIGURE 6



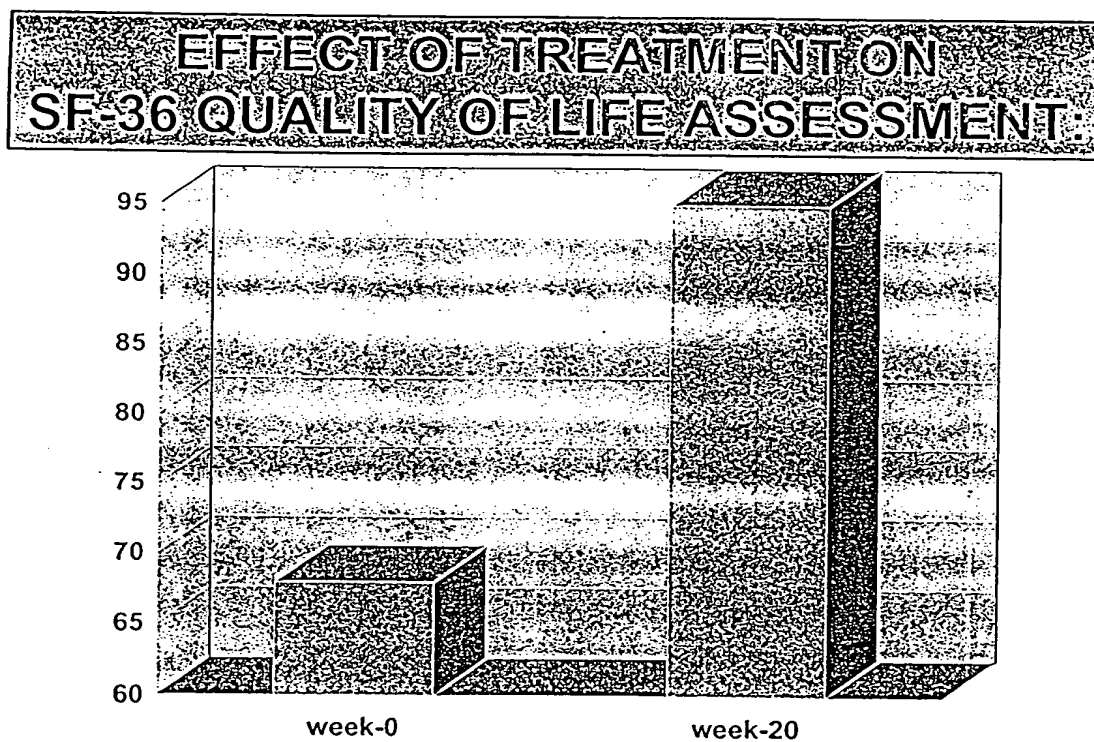
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FIGURE 7



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FIGURE 8



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